

IN THE CLAIMS:

We claim:

1. (Currently Amended) A method of isolating clones comprising a polynucleotide of a microbe or pathogen that is expressed only *in vivo* comprising:
 - (a) obtaining an antibody sample from one or more hosts naturally infected with the microbe or pathogen;
 - (b) adsorbing the antibody sample with *in vitro* grown cells or cellular extracts of the microbe or pathogen ~~that have been grown *in vitro*~~;
 - (c) isolating unadsorbed antibodies; and
 - (d) probing an expression library of clones of the microbe or pathogen with the unadsorbed antibodies of (c) and isolating clones from the expression library to which the unadsorbed antibodies bind;
wherein clones comprising a polynucleotide of the microbe or pathogen that is expressed only *in vivo* are isolated.
2. (Currently Amended) The method of claim 1 wherein the polynucleotides of the microbe or pathogen that are expressed only *in vivo* ~~encodes~~ encode *in vivo* induced antigens.
3. (Previously Presented) The method of claim 2 wherein the *in vivo* induced antigens are capable of eliciting an immune response in an animal.
4. (Previously Presented) The method of claim 3 wherein the animal is selected from the group consisting of humans, baboons, chimpanzees, macaques, cattle, sheep, pigs, horses, goats, dogs, cats, rabbits, guinea pigs, rats, mice, chickens, ducks, and fish.
5. (Original) The method of claim 1 further comprising the step of determining the nucleic acid sequence of the polynucleotide.
6. (Withdrawn) A method of confirming the isolated polynucleotide of claim 1 as expressed only *in vivo* comprising:

- (a) expressing and isolating a polypeptide from the isolated polynucleotide of claim 1;
- (b) producing antibodies to the polypeptide; and
- (c) demonstrating that the antibodies are reactive with biological samples from disease sites from a host infected with the microbe or pathogen, but not reactive with cells or cellular extracts of the microbe or pathogen that have been grown *in vitro*;
- whereby the isolated polynucleotide is confirmed as being expressed only *in vivo*.
7. (Previously Presented) The method of claim 1 wherein the antibody sample of (a) is sera from the one or more hosts infected with the microbe or pathogen.
8. (Previously Presented) The method of claim 1 wherein the microbe or pathogen is selected from the group consisting of a bacterium, a virus, a parasite, a prion, and a fungus.
9. (Previously Presented) The method of claim 1 wherein the microbe or pathogen is selected from the group consisting of *Candida*, *Aspergillus*, *Sporothrix*, *Blastomyces*, *Histoplasma*, *Cryptococcus*, *Pneumocystis*, *Coccidioides*, *Tinea*, *Toxoplasma*, *Plasmodium*, *Pseudomonas*, *Actinobacillus*, *Staphylococcus*, *Bacillus*, *Clostridium*, *Listeria*, *Corynebacterium*, *Actinomyces*, *Mycoplasma*, *Nocardia*, *Bordetella*, *Brucella*, *Francisella*, *Legionella*, *Enterobacter*, *Escherichia*, *Klebsiella*, *Proteus*, *Salmonella*, *Shigella*, *Streptococcus*, *Yersinia*, *Vibrio*, *Campylobacter*, *Helicobacter*, *Bacteroides*, *Chlamydia*, *Borrelia*, *Treponema*, *Leptospira*, *Aeromonas*, *Rickettsia*, *Ascari*, *Cryptosporidium*, *Cyclospora*, *Entamoeba*, *Giardia*, *Shistosoma*, *Trypanosoma*, herpes virus, cytomegalovirus, Epstein-Barr virus, hepatitis virus, adenovirus, papillomavirus, polyomavirus, enterovirus, rotavirus, influenza virus, paramyxovirus, rubeola virus, rhabdovirus, human immunodeficiency virus, arenavirus, rhinovirus, and reovirus.

10. (Previously Presented) The method of claim 7, wherein the one or more hosts are an animal selected from the group consisting of humans, baboons, chimpanzees, macaques, cattle, sheep, pigs, horses, goats, dogs, cats, rabbits, guinea pigs, rats, mice, chickens, ducks, and fish.
11. (Withdrawn) A method of comparing polynucleotides of a microbe or pathogen that are expressed only *in vivo* and at different stages of infection of the microbe or pathogen comprising the steps of:
- (a) obtaining a first antibody sample from one or more hosts infected with the microbe or pathogen, wherein each host is in about the same stage of the infection;
 - (b) adsorbing the first antibody sample with cells or cellular extracts of the microbe or pathogen that have been grown *in vitro*;
 - (c) obtaining a second antibody sample from one or more hosts infected with the microbe or pathogen, wherein each host is in about the same stage of the infection, wherein the stage of the infection is different from the stage of infection in step (a);
 - (d) adsorbing a the second antibody sample with cells or cellular extracts of the microbe or pathogen that have been grown *in vitro*;
 - (e) isolating unadsorbed antibodies from the first antibody sample and from the second antibody sample;
 - (f) probing a first expression library of clones of the microbe or pathogen with the unadsorbed antibodies from the first antibody sample and isolating clones from the first expression library to which the unadsorbed antibodies bind, and probing a second expression library of clones of the microbe or pathogen with the unadsorbed antibodies from the second antibody sample and isolating clones from the second expression library to which the unadsorbed antibodies bind, wherein polynucleotides of the microbe or pathogen that are expressed only *in vivo* are isolated for the first and second antibody sample; and

- (g) comparing the polynucleotides of the microbe or pathogen that are expressed only *in vivo* and at different stages of infection of the microbe or pathogen.
12. (Withdrawn) The method of claim 11 wherein the first expression library and the second expression library are the same expression library.
13. (Withdrawn) A method of comparing polynucleotides of a microbe or pathogen that are expressed only *in vivo*, wherein the microbe or pathogen has infected its host by different routes of infection comprising the steps of:
- (a) obtaining a first antibody sample from one or more hosts infected with the microbe or pathogen, wherein each host has been infected by about the same route of infection;
 - (b) adsorbing the first antibody sample with cells or cellular extracts of the microbe or pathogen that have been grown *in vitro*;
 - (c) obtaining a second antibody sample from one or more hosts infected with the microbe or pathogen, wherein each host has been infected by about the same route of infection, wherein the route of infection is different from the route of infection in step (a);
 - (d) adsorbing the second antibody sample with cells or cellular extracts of the microbe or pathogen that have been grown *in vitro*;
 - (e) isolating unadsorbed antibodies from the first antibody sample and from the second antibody sample;
 - (f) probing a first expression library of clones of the microbe or pathogen with the unadsorbed antibodies from the first antibody sample and isolating clones from the first expression library to which the unadsorbed antibodies bind, and probing a second expression library of clones of the microbe or pathogen with the unadsorbed antibodies from the second antibody sample and isolating clones from the second expression library to which the unadsorbed antibodies bind, wherein polynucleotides of the microbe or pathogen that are expressed *in vivo* are isolated for the first and second antibody sample; and

- (g) comparing the polynucleotides of the microbe or pathogen that are expressed only *in vivo* by different routes of infection of the microbe or pathogen.
14. (Withdrawn) The method of claim 13 wherein the first expression library and the second expression library are the same expression library.
15. (Withdrawn) A method of confirming an animal model of infection as a valid model comprising the steps of:
- (a) obtaining a first antibody sample from one or more first animal model hosts infected with a microbe or pathogen;
 - (b) adsorbing the first antibody sample with cells or cellular extracts of the microbe or pathogen that have been grown *in vitro*;
 - (c) obtaining a second antibody sample from one or more second hosts infected with the microbe or pathogen, wherein the second host is a different species of animal than the first animal model host;
 - (d) adsorbing a the second antibody sample with cells or cellular extracts of the microbe or pathogen that have been grown *in vitro*;
 - (e) isolating unadsorbed antibodies from the first antibody sample and from the second antibody sample;
 - (f) probing a first expression library of clones of the microbe or pathogen with the unadsorbed antibodies from the first antibody sample and isolating clones from the first expression library to which the unadsorbed antibodies bind, and probing a second expression library of clones of the microbe or pathogen with the unadsorbed antibodies from the second antibody sample and isolating clones from the second expression library to which the unadsorbed antibodies bind, wherein polynucleotides of the microbe or pathogen that are expressed only *in vivo* are isolated for the first and second antibody sample; and
 - (g) comparing the polynucleotides of the microbe or pathogen that are expressed only *in vivo* in the first animal model host and the second host;

- wherein if the polynucleotides expressed only *in vivo* in the first animal model and in the second host are the same or similar, then the first animal model is confirmed as a valid model.
16. (Withdrawn) The method of claim 15 wherein the first expression library and the second expression library are the same expression library.
 17. (Withdrawn) The method of claim 15 wherein the first animal model host and the second host are selected from the group consisting of humans, baboons, chimpanzees, macaques, cattle, sheep, pigs, horses, goats, dogs, cats, rabbits, guinea pigs, rats, mice, chickens, ducks, and fish.
 18. (Canceled)
 19. (Canceled)
 20. (Previously Presented) The method of claim 1, wherein the microbe is a bacterium or a fungus.
 21. (Canceled)
 22. (Canceled)
 23. (Canceled)
 24. (Canceled)
 25. (Canceled)
 26. (Previously Presented) The method of claim 1, wherein the one or more hosts infected with the microbe or pathogen is a human.
 27. (Canceled)
 28. (Canceled)
 29. (New) The method of claim 1, wherein an antibody sample is obtained from more than one host naturally infected with the microbe or pathogen and wherein the hosts are infected by the pathogen by more than one route of infection.
 30. (New) The method of claim 1, wherein an antibody sample is obtained from more than one host naturally infected with the microbe or pathogen and wherein the hosts are in different phases of infection by the pathogen.
 31. (New) The method of claim 1, wherein an antibody sample is obtained from more than one host naturally infected with the microbe or pathogen and

wherein the hosts are infected by different clonal variants or different strains of the pathogen.